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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,430	01/17/2002	Mathieu Hubertus Maria Noteborn	2906-4992US	2965

7590 07/30/2003

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EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/889,430	NOTEBORN ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-36* is/are pending in the application.

4a) Of the above claim(s) *17,18,27-30 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-26,31 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II without traverse and species election drawn to apoptin as the apoptosis inducing agent and viral vector as means of targeting in Paper No. 11 is acknowledged. Claims 17-36 are pending. Claims 17, 18, 27-30, and 32 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Claims 19-26, 31, and 33-36 are under current examination.

Specification

The specification contains sequence disclosures (page 12, lines 31-32) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) but are not identified in the specification by sequence identifier numbers. Applicant must provide sequence identifiers, in the case that these sequences are not included in the original sequence submission, a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office Action must include a complete response to the requirement for a Sequence Listing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 21, 23-25, 31, and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings, or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

The claims are directed to a method for treating an inflammatory disorder or an immune disease in a subject comprising administering to the subject a gene delivery

vehicle expressing an apoptosis-inducing agent exhibiting its effect in aberrant cells involved or related to immune disease, wherein the gene delivery vehicle has a *tropism* for hematopoietic cells or fibroblast-like synoviocytes, or is provided with a *targeting means*. Given the broadest reasonable interpretation, the claims read on a therapeutic method for treating any and all inflammatory disorder or immune disease using a gene delivery vehicle capable of targeting any aberrant cell population. However, the specification fails to provide an adequate disclosure for the genus of the claimed invention in terms of distinguishing characteristics of the genus of targeting means.

The specification prophetically teaches that in order to reduce unwanted effects of the gene delivery vehicles, it is preferred the vehicle has or is provided with a tropism for its target cells and this could be done by simply selecting a gene delivery vehicle that has such a tropism or if none such a vehicle is available, it can be provided through phage display screening of random sequences having affinity for the target cells (paragraph bridging pages 4 & 5). However, the specification fails to teach the preferred target cell population for each of the numerous diseases encompassed by the claims, the specification fails to teach that if the screening of random sequences is needed, the suitable target to screen for, and the proper starting materials to screen with. In fact, the specification fails to teach any gene delivery vehicle that has the recited tropism, and the only specific vehicle recited in the claims and specification as the preferred embodiment is the adenoviral vector, which is known to have a tissue tropism for airway epithelium and liver cells (US 6,475,480, column 1, lines 42-44), not hematopoietic or synovial cells. Therefore, the specification fails to provide an adequate description for

the gene delivery vehicle having a tropism for hematopoietic cells or fibroblast-like synoviocytes, and it fails to provide an adequate description for any targeting means for any cell associated with any immune or inflammatory disorders, and accordingly does not provide a reasonable guide for those seeking to practice the invention.

An adequate written description for a gene delivery vehicle having a specific targeting means requires more than a mere statement that it is part of the invention; what is required is a description of the vehicle itself. It is not sufficient to define the vehicle solely by its principal biological property, i.e. "**has a tissue tropism for hematopoietic cells**" or "**has a tissue tropism for fibroblast-like synoviocytes**", because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any gene delivery vehicle with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all vehicles that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific chemical structure and physical properties of the material, which provide the means for practicing the invention. The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER

THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad classes of *gene delivering vehicle having a tropism for hematopoietic cells or synoviocytes or any targeting means*". Therefore, the specification fails to meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

To the extent that the claimed invention is not adequately described in the instant disclosure, claims 19, 20, 21, 23-25, 31, and 33-35 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been adequately described.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

One cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan cannot envision the detailed structures of gene delivery vehicle having a specific targeting means encompassed by these claims, thus, one would not know how to use the invention without first carrying out undue experimentation to determine what is the proper target for a specific tissue tropism, how to provide such, and what random sequences to start with when searching for a proper target means. Therefore, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-26, 31, and 33-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because they provide a method for treating an immune disease, however, there is no positive step or recitation that clearly relates back to the preamble to indicate that the goal of the method is resolved.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 19, 20, and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by *Sata et al* (PNAS 1998 Feb;95:1213-7).

Claims are drawn to a method of treating an inflammatory disorder or an immune disease comprising administering to a subject a gene delivery vehicle expressing an apoptosis-inducing agent, wherein the vehicle comprises a recombinant adenovirus.

The specification fails to define the term "inflammatory disorder" or "immune disease", thus, given the plain meaning of the term in the relevant art, inflammatory disorders encompass any disorder having a localized protective reaction of tissue irritation, injury or infection, and immune disease encompasses any disease associated with the immune system, such as injury, allergy, autoimmune, graft rejection, infection, and tumor.

Sata et al teach a method comprising administering locally to balloon-injured rat carotid arteries a recombinant adenoviral vector encoding and expressing FasL (an apoptosis-inducing agent), which inhibit the robust T cell infiltration of the vessel wall (e.g. abstract). Therefore, *Sata et al* anticipate instant claims.

Claims 19, and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by *Li et al* (Transplant 1998;66:1416-23).

Li et al teach a method comprising transplanting allogeneic liver cells transfected with a recombinant plasmid vector encoding and expressing FasL (administering a gene delivery vehicle comprising a gene capable of expressing an apoptosis-inducing agent), which prolong the survival of the allograft (e.g. abstract, treating immune rejection response). Therefore, *Li et al* anticipate instant claims.

Claims 19, 20, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by *WO 97/07828*.

WO 97/07828 teaches a method for treating inflammatory disease, specially rheumatoid arthritis comprising administering to a patient a recombinant vector encoding and expressing apoptosis-inducing agents such as p53, ICE, bax, p21waf, and ras (abstract, and claims 1-20), wherein the vector is recombinant adenoviral vector (claim 11). Therefore, *WO 97/07828* anticipates instant claims.

Claims 19, 20, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by *Zhang et al* (Arthritis & Rheumatism 1997;40(9):S294).

Zhang et al teach a method for treating inflammatory arthritis in an animal model, comprising administering to the inflammed joint a recombinant adenoviral vector encoding and expressing apoptosis-inducing agents FasL. Therefore, *Zhang et al* anticipate instant claims.

Claims 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by *Arai et al* (Nat Med 1997;3:843-8).

Arai et al teach a method comprising administering subcutaneously to C57BL/6 mice CT26 cells transfected with a recombinant plasmid vector encoding and expressing CD95L (an apoptosis-inducing agent), which markedly reduced allogeneic cytotoxic T lymphocyte response and alloantibody responses (e.g. abstract). Therefore, *Arai et al* anticipate instant claims.

Claims 19, 20, 21, 26, and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by *McCormick et al* (US 5,801,029).

Claim 21 is directed to a gene delivery vehicle expressing both an apoptosis inducing agent and a suicide gene.

McCormick et al teach a method comprising administering to a subject mutant viruses (an apoptosis-inducing agent), which preferentially replicate in neoplastic cells and inducing apoptotic cell death in these cells (abstract and column 6, lines 11-13). *McCormick et al* goes on to teach that the virus is adenovirus optionally expressing a cytopathic gene e.g. HSV tk (suicide gene, column 3, lines 21-25 and paragraph bridging columns 14 and 15) Therefore, *McCormick et al* anticipate instant claims.

Claims 19 and 20 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/733,416 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

The claims of the present application and the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of apoptin derivatives specifically whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin. Therefore, the instant claims encompass claims of the cited patent application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Claims 19 and 20 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent application 09/746,176.

Claims 19 and 20 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/746,176 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

The claims of the present application and the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of apoptin specifically whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin. Therefore, the instant claims encompass claims of the cited patent application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Claims 19 and 20 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent application 09/819,308.

Claims 19 and 20 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/819,308 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e)

is based upon a presumption of future publication or patenting of the copending application.

The claims of the present application and the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of a specific apoptin and fragment thereof whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin. Therefore, the instant claims encompass claims of the cited patent application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Claims 19 and 20 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The subject matter as claimed encompasses that of claims 27 and 28 of U.S. patent application 09/733,416, which has a different inventive entity. Further clarification is required as to who is the real inventor.

Claims 19 and 20 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The subject matter as claimed encompasses that of claims 17 and 24 of U.S. patent application 09/764,176, which has a different inventive entity. Further clarification is required as to who is the real inventor.

Claims 19 and 20 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The subject matter as claimed encompass that of claims 15 and 19 of U.S. patent application 09/819,308, which has a different inventive entity. Further clarification is required as to who is the real inventor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Sata et al* (PNAS 1998 Feb;95:1213-7), in view of *Zuckermann et al* (US 6,468,986).

Claims are drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis-inducing agent, wherein the vehicle comprises a recombinant adenovirus, wherein the agent is apoptin.

Sata et al teach a method comprising administering locally to balloon-injured rat carotid arteries a recombinant adenoviral vector encoding and expressing FasL (an apoptosis-inducing agent), which inhibit the robust T cell infiltration of the vessel wall (e.g. abstract). *Sata et al* teach that FasL-Fas system has been implicated in the regulation of physiological cell turnover, particularly in the immune system and could be used to alter the T cell response (Introduction), that the inflammatory fibroproliferative disorders of the vessel wall provide a unique system to explore the therapeutic utility of FasL. *Sata et al* does not particularly teach an apoptin as the apoptosis-inducing agent.

Zuckermann et al teach that apoptin is one of the pro-apoptotic agent as is FasL (column 12, line 13).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Sata et al,* by substituting or combining the apoptin in the gene delivery vehicle as taught by *Zuckermann et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to make the modification because it is within the knowledge of the skill to select one of the known apoptosis-inducing agents in the art for suppressing unwanted cell proliferation. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 19, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over *McCormick et al* (US 5,801,029), and in view of *Bujard et al* (US 5,814,618).

Claim 22 is directed to expressing a suicide gene in an inducible manner.

McCormick et al teach a method comprising administering to a subject mutant viruses (an apoptosis-inducing agent), which preferentially replicate in neoplastic cells and inducing apoptotic cell death in these cells (abstract and column 6, lines 11-13). *McCormick et al* goes on to teach that the virus is adenovirus optionally expressing a cytopathic gene e.g. HSV tk (suicide gene, column 3, lines 21-25 and paragraph bridging columns 14 and 15). *McCormick et al* do not particularly teach that the tk gene is expressed in an inducible manner.

Bujard et al teach an inducible promoter system (abstract) that could be used for regulating gene expression, such as TK gene, so that the suicide gene could be expressed in a controlled manner and the inducible promoter adds safety to the use of a suicide gene (column 39, lines 57-66).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *McCormick et al,* by using an inducible promoter for controlling the expression of a suicide gene in the gene delivery vehicle as taught by *Bujard et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to make the modification because it adds to the general safety and usefulness of the suicide gene. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 and 25 of copending Application No. 09/403,213. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass claims 22 and 25 of the cited patent application.

The claims of the present application and that of the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in the preamble recitation, i.e. “inflammatory disorder” vs. “tumor”. However, the specification fails to define the term “inflammatory disorder”, given the broadest reasonable interpretation, tumor is caused by disorders of immune system and exhibits inflammation at the site of the tumor, thus, the term “inflammatory disorder” or “immune disease” would encompass “tumor”.

Accordingly, the claimed processes in the copending and the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17 and 24 of copending Application No. 09/764,176. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass claims 17 and 24 of the cited patent application.

The claims of the present application and that of the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of apoptin specifically whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin.

Accordingly, the claimed processes in the copending and the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15 and 19 of copending Application No. 09/819,308. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass claims 15 and 19 of the cited patent application.

The claims of the present application and that of the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of apoptin specifically whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin.

Accordingly, the claimed processes in the copending and the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27 and 28 of copending Application No. 09/733,416. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass claims 27 and 28 of the cited patent application.

The claims of the present application and that of the cited patent application are each drawn to a method comprising administering to a subject a gene delivery vehicle expressing an apoptosis inducing agent exhibiting its effect in aberrant cells.

The processes of the present application and the cited patent application differ one from the other in that the claims of the cited patent application are drawn to delivery of apoptin and derivatives specifically whereas instant claims broadly encompass delivering any apoptosis inducing agent, including apoptin and its derivatives.

Accordingly, the claimed processes in the copending and the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
July 25, 2003